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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,005	03/28/2006	Georg Sczakiel	195.66	9324

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,005	SCZAKIEL ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Russia on 08/18/2003. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter. Accordingly, Applicant is afforded the instant filing date of March 28, 2006.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "a method for detecting cell surface bound extracellular nucleic acids in blood plasma of patients with lung, breast or colon cancers or a method of detecting cell surface bound extracellular nucleic acids in pregnant patients or pregnant patients with preeclampsia, it does not reasonably provide enablement for a method for the early diagnosis of a diseases in a human induced by abnormal functioning of cellular genome as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when

determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is "undue". These factors include but are not limited to: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented in the specification, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the unpredictability of the art and (8) the breadth of the claims. (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)) *(MPEP 2164.01(a))*. The claims are broadly drawn to a method for the early diagnosis of diseases in a human induced by abnormal functioning of cellular genomes, the steps of the method comprising: (a) sampling blood of the human; (b) dividing the blood into plasma and cellular fractions; (c) dividing the blood into plasma and cellular fractions; (c) isolating extracellular nucleic acids (exNA); and (d) revealing species sequence of nucleic acids by means of polymerase chain reaction. The invention is in a class of invention which the Court of Appeal of the Federal Circuit has characterized as "the unpredictable arts such as chemistry and biology". *Mycogen Plant Sci., Inc. v. Monsanto Co.,* 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The specification teaches at page 2 that the object of the invention to provide a method of early detection and monitoring of diseases. The specification further teaches in Table 1 increase amount of extracellular and cell-surface bound nucleic acids in blood sample from patients with lung cancer versus healthy donors. In Table 2, the specification teaches the frequency of cell-surface bound DNA in c-myc and c-erbB2

expression in patients with breast cancer and in Table 3, the specification teaches the frequency of cell surface bound nucleic acid and plasma DNA in CK19 and CEA genes expression in patients versus healthy donors.

The specification however does not teach any method steps for the diagnosis of any diseases or an early diagnosis of any diseases as broadly encompassed by the claims. There is no data or evidence to support any early detection of any disease, such as cancers of the head and neck or prostate cancer or diabetes or cardiovascular diseases or inflammatory diseases, such HIV or many of the plethora of diseases encompassed by the claims as broadly written. Likewise, the data provided therein in the Tables 1-3 do not provide any evidence of any early diagnosis of any disease, including lung, breast and colon cancers; but rather teaches detection of cell surface bound extracellular nucleic acids in gene markers associated lung cancer, breast cancer or colon cancer versus control samples. Likewise, the specification does not provide any guidance or working examples to practice the invention fully in scope. As to unpredictability in the art, while the art supports detecting extracellular DNA in breast cancer and nonmalignant tumors (Rykova et al., Ann. N.Y. Acad. Sci., 1022: 217-220, June 2004), the art does support diagnosing any of the plethora of diseases known in the art.

Case law has established that "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'". *In re Wright* 990 F.2d 1557, 1561. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "[t]he

scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the *Court in Genetech Inc. v. Novo Nordisk* 42 USPQ2d 1001 held that "[I}t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". Thus, undue experimentation is deemed necessary to practice the invention fully in scope.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The claims 1-4 are generally narrative and indefinite, thus making a clear interpretation difficult. For example, the step (d) is extremely confusing and a relationship or nexus between the steps (a) through (c) and the "wherein clause" in step (d) cannot be ascertained. It is suggested amending the claims such that applicants' intents are clearly recited.

(b) Claim 2 is confusing at in step (a) because it cannot be determined what is meant by "providing a two-step elution" and what method steps are required for "a two

step elution". The claims are further confusing at the recitation of "supplied with 5mM EDTA" because it cannot be determine if the PBS was made by using 5mM EDTA or if the PBS solution comprises 5 mM EDTA or if reference is being made to a dilution to obtain the 10 volumes of PBS. Clarification is required.

(c) Claim 3 is confusing at "increased glass milk protocol" because it is unclear as to what is meant by "increased glass milk protocol" or what steps are required to perform the claimed increased glass milk protocol. Clarification is required.

Claim Rejections - 35 USC § 102

Note* The claims of the instant invention are extremely broad and overly wordy. Therefore, the preceding rejections are based on the Examiner's best interpretation of the claims as currently written.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Rykova et al (Ann. N.Y. Acad. Sci. 1022: 217-220, June 2004). Regarding claim 1, Rykova et al teach a method comprising sampling a blood of the human, dividing the blood into plasma and cellular fractions, isolating exctracellular nucleic acid (exNA) and revealing

specific sequences of nucleic acid by means of polymerase chain reaction with subsequent analysis of the presence or absence of specific sequence in total PCR products, whereby cell surface bound extracellular nucleic acids are used as a source of extracellular nucleic acids instead of extracellular nucleic acid from plasma fraction, and whereby the cellular fraction is divided into leukocytes and erythrocytes, cell bound surface extracellular nucleic acids are subsequently eluted from cell surface, exNA are isolated from elutes and these exNA are used for analysis of at least two specific sequences of exNA distinctive for a disease (Abstract and page 218, section entitled "Material and Methods" and Figure 1).

Regarding claim 2, Rykova et al teach wherein the method comprises providing a two-stage elution of exNA from the surface of leukocytes; eluting exNA by treatment of cells with 10 volume of PBS comprising 10mM EDTA, pelleting the cells by centrifugation and collecting the supernatant; eluting if exNA with 0.25% trypsin solution; inactivating of an enzyme with trypsin inhibitor and centrifugation collection of supernatant (page 218, "materials and Method").

Regarding claim 3, Rykova et al teach wherein exNA is isolated by means of a glass milk protocol (page 218 last paragraph).

Regarding claim 4, Rykova et al teach wherein early detection of cancer is indicated. Therefore, Rykova et al meets the limitations of the claims as currently written.

8. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Gocke et al (WO 97/34015, September 1997). Regarding claim 1, Gocke et al teach a

method comprising sampling a blood of the human, dividing the blood into plasma and cellular fractions, isolating exctracellular nucleic acid (exNA) and revealing specific sequences of nucleic acid by means of polymerase chain reaction with subsequent analysis of the presence or absence of specific sequence in total PCR products, whereby cell surface bound extracellular nucleic acids are used as a source of extracellular nucleic acids instead of extracellular nucleic acid from plasma fraction, and whereby the cellular fraction is divided into leukocytes and erythrocytes, cell bound surface extracellular nucleic acids are subsequently eluted from cell surface, exNA are isolated from elutes and these exNA are used for analysis of at least two specific sequences of exNA distinctive for a disease (see pages 18-29).

Regarding claim 4, Gocke et al teach wherein early detection of cancer is indicated (see Examples beginning at page 35). Therefore, Gocke et al meets the limitations of the claims recited above.

Information Disclosure Statement

9. The information disclosure statement filed on 3/26/2006 is acknowledged. However, a copy of the foreign document recited therein could not found in the instant application and therefore could not be considered. It is suggested submitting the foreign document for consideration along with a translation if necessary.

Conclusion

10. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D.

whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1637
4/11/2007